

SUPPORT FOR THE AMENDMENTS

Claims 1, 3-14, 17, 20, and 21 have been amended.

Claims 22-31 have been added.

Support for the amendment of Claims 1, 3-14, 17, 20, and 21 and for new Claims 22-31 is provided by original Claims 1-21. New Claims 22, 30, and 31 correspond to withdrawn subject matter.

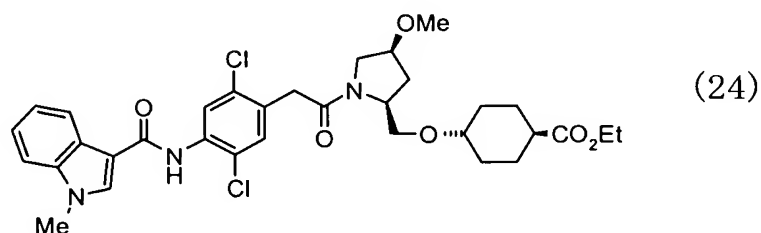
No new matter has been added by the present amendment.

REMARKS

Claims 1-31 are pending in the present application.

The rejection of Claims 1-7, 9, and 20 under 35 U.S.C. §103(a) over Nakayama et al (WO 02/053534 (cited as equivalent of US 2003/0134859, now US 7,157,487)) in view of March (March's Advanced Organic Chemistry 5th Ed. (2001)) is respectfully traversed.

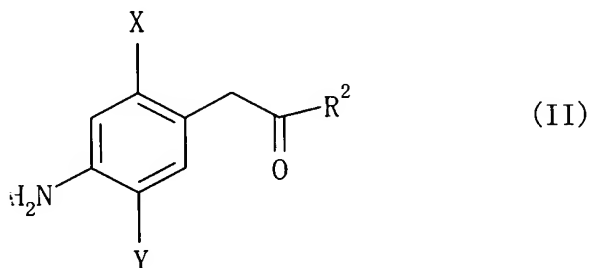
The elected invention is drawn to a method of producing a compound of Formula III and the elected species is the compound of Example 14, which is described at section (3-1) or (3-2) in paragraph [0193] or [0194]. Specifically, the elected species is the compound of formula (24) below:



As properly recognized, the claimed method involves reacting a compound represented by formula (I):



with a chlorinating agent and a compound represented by formula (II):



However, this is where the Examiner's proper recognition appears to end. Specifically, the Examiner cites the generic process in scheme 1C (columns 49-51) of Nakayama et al, as well as the specific methods disclosed in column 233 (step (3) of Example 66) and column 294 (step (1) of Example 90) as allegedly being relevant to the claimed method. Applicants disagree with the Examiner that the disclosure of Nakayama et al as discloses that an amide bond may be formed in the presence of an acid and utilizing an acid halide as a chlorinating agent. None of the sections of the Nakayama et al referred to by the Examiner relate to reacting a compound represented by formula (I) as defined in the claimed invention with a chlorinating agent and a compound represented by formula (II) as defined in the claimed invention.

As one of the characteristic features of the claimed invention, there is an acidic condition under which an amidation step is carried out in association with Compound (1) and Compound (II). Compared with the method disclosed in Nakayama et al, this step has great advantages that can make it possible not only to block a dimer of the carboxylic acid from emerging as a by-product, but also to skip an additional step that would otherwise be needed, to isolate acid chlorides (see paragraphs [0013], [0103] and [0104]).

The Examiner alleges that no substantial difference can be recognized in the reaction condition of the elected species of Example 14 compared with the step 3 described in Example 66 of Nakayama et al. However, in the elected species of Example 14 the reaction system is required to be acidic, whereas the reaction system of Nakayama et al is required to be basic.

As can be seen from Example 14 (3-1) of the present application, oxalyl chloride (1.2 mole-eq.) is allowed to react with carboxylic acid, by which hydrochloride (2.4 mole-eq.) is produced, and triethylamine (1.3 mole-eq.) is added directly to the reaction mixture.

Accordingly, the reaction mixture of the present invention is clearly acidic overall. The other Examples also show the same condition. For instance, Example 5 gives another example in which base is not used and the reaction mixture is made acidic by the hydrochloride derived from oxalyl chloride.

In direct contrast, Step 3 of Example 66 disclosed by Nakayama et al describes that oxalyl chloride is reacted with a carboxylic acid. After the reaction solvent is distilled off, triethylamine is added to the reaction mixture. Therefore, the reaction mixture of Nakayama et al is *basic*.

The Examiner cites March as disclosing related well known methods of forming amides in a synthetic scheme. The Examiner merely states that “One of ordinary skill in the art of organic synthesis would be well versed in the teachings of references such as March. One of ordinary skill in the art would consider routine and well within their technical grasp the process of altering reaction conditions to maximize yield. In addition, those of ordinary skill in the art would first look to known synthetic methods in the art that share structural elements with the object of the endeavor.” However, all the Examiner provides is this very general allegation. The Examiner is reminded that when an Examiner maintains that there is an implicit teaching or suggestion in the prior art, “the Examiner should indicate where (page and line or figure) such a teaching or suggestion appears in the prior art.” *Ex parte Jones*, 62 USPQ2d 1206, 1208 (Bd. Pat. App. & Inter. 2001) The Examiner has clearly failed to meet this burden.

Nonetheless, Applicants submit that although March discloses a similar amidation step (see the paragraph bridging between pages 506 and 507), there is no doubt that the step is performed under a *basic* condition. Specifically, this reference describes as follows: “In some case aqueous alkali is added to combine with the liberated HCl” (see the last line of

page 506 to the first line of page 507). In other words, when HCl is liberated the reaction system becomes acid and therefore makes little or no progress, so that it becomes necessary to add base to the reaction mixture in order to avert such a consequence (Schotten-Baumann Method).

The combined disclosures could be taken as an “invitation to experiment” or could be viewed as providing an “obvious to try” argument; however, “obvious to try” has long been held *not* to constitute obviousness. *In re O'Farrell*, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).

Thus, Applicants submit that there is no disclosure or suggestion in Nakayama et al and/or March to modify the method of Nakayama et al to arrive at the presently claimed method and certainly there can be no reasonable expectation of success.

Withdrawal of this ground of rejection is requested.

The objection to Claims 4-7, 9, and 20 as being improper multiple dependent claims is obviated by amendment herein. Applicants have amended the claims to remove all multiple dependencies. Withdrawal of this ground of objection is requested.

With respect to the elected species, Applicants submit that the election was provisional and only to facilitate examination. Applicants respectfully submit that, should the elected species be found allowable, the Office should expand its search to the non-elected species.

Applicants also remind the Examiner of the possibility of rejoinder of the non-elected method claim in accordance with MPEP §821.04.

Applicants submit that the present application is now in condition for allowance.
Early notification of such action is earnestly solicited.

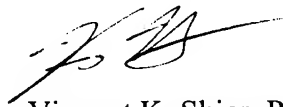
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